Ductular bilirubinostasis predicts the evolution to acute-on-chronic liver failure in patients suspected with severe alcoholic steatohepatitis

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Introduction

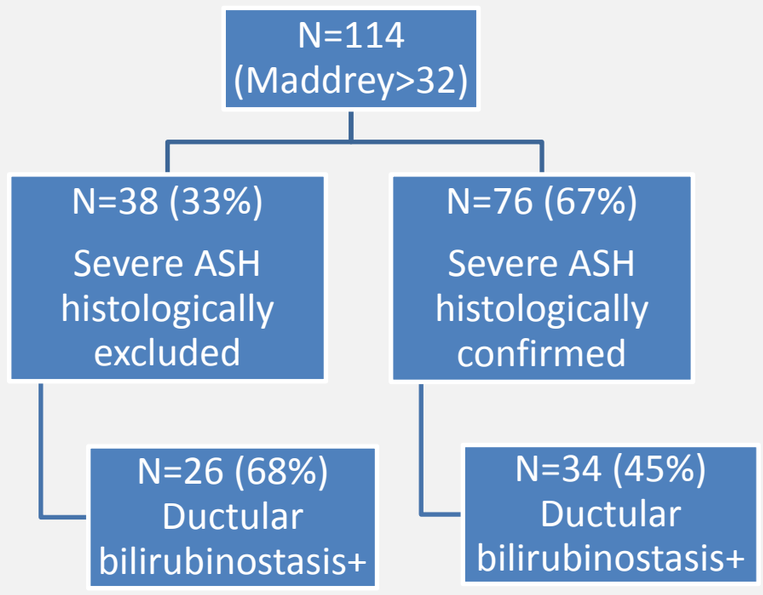
- Current EASL guidelines consider a liver biopsy optional to diagnose severe alcoholic steatohepatitis (ASH).
- Based on clinical criteria (i.e. Maddrey-score / MDF ≥32) patients are initiated on corticosteroids (CS) *(EASL guidelines 2012)*.
- In patients with acute decompensation of alcoholic cirrhosis, making a diagnosis of ASH on clinical grounds may be challenging, since it resembles acute-on-chronic liver failure (ACLF).
- We recently identified ductular bilirubinostasis (DB) as an early risk factor for ACLF[1].

[1]Katoonizadeh et al. Gut 2010

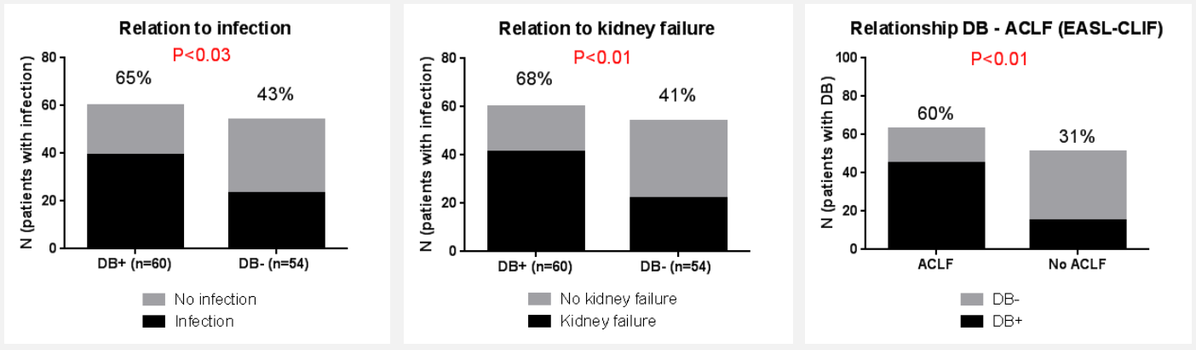
Methods

- Prospective trial of 114 patients with alcoholic cirrhosis and suspicion of severe ASH (i.e. MDF ≥32) who underwent a transjugular liver biopsy within 3 days after admission.
- Literature-reported clinical, biochemical and histological parameters indicative of severe ASH and/or ACLF were assessed and correlated to the risk of death and the response to CS using logistic regression and survival analysis.

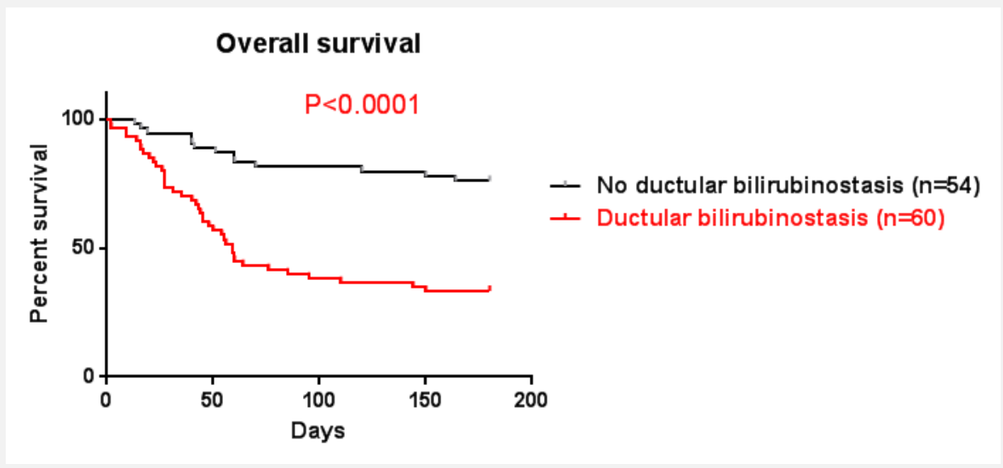
Results I

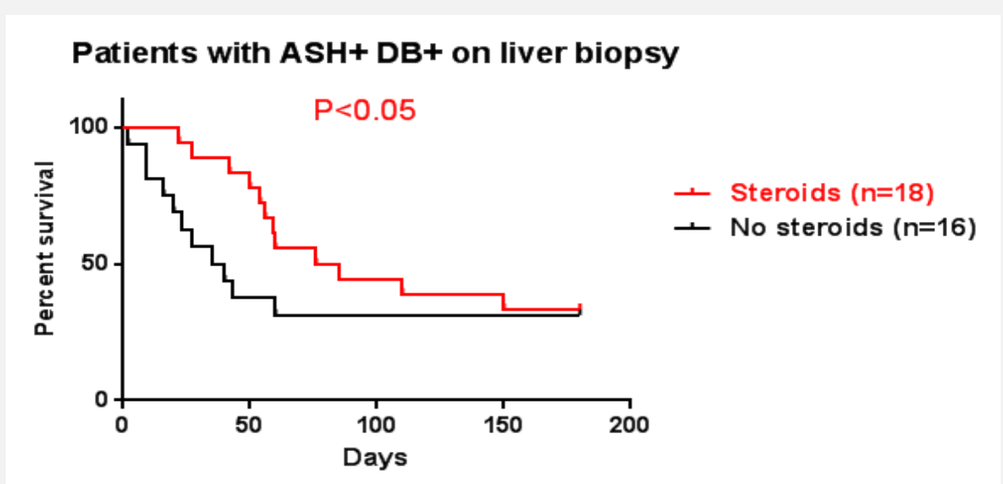


Results III – Ductular bilirubinostasis on early liver biopsy and correlation with infection, kidney failure and ALCF



Results IV – Survival





Results II – Clinical characteristics

** *EASL-CLIF criteria*

	ASH+ DB+ (n=34)	ASH+ DB- (n=42)	ASH- DB+ (n=26)	ASH- DB- (n=12)	P-value (between groups)
Sex (m/f)	23/11	20/22	14/12	6/6	0.35
Age (years)	52±2	50±2	54±2	54±2	0.54
Alcohol intake (grams/day)	82±4	88±3	68±5	75±8	0.25
HVPG (mm Hg)	18.3±1.4	19.0±1.0	18.3±1.3	16.5±0.75	0.77
SIRS	62% (21/34)	48% (20/42)	65% (17/26)	58% (7/12)	0.46
Infection at/during admission	65% (22/34)	43% (18/42)	65% (17/26)	42% (5/12)	0.12
Plasma bilirubin at admission (mg/dl)	19.1±1.4	18.7±1.8	16.8±2.1	7.3±1.0	**P<0.01**
MDF	60±5.0	56±3.7	51±4.0	46±3.2	0.31
MELD	28.8±1.4	26.3±1.0	26.7±0.8	22.3 ± 1.2	**0.02**
% CS-treated	53% (18/34)	69% (29/42)	27% (7/26)	17% (2/12)	<0.0001
Lille-score <0.45 (after CS)	44% (8/18)	72% (21/29)	43% (3/7)	50% (1/2)	0.21
% Evolution towards ACLF**	88% (30/34)	56% (17/42)	81% (21/26)	75% (3/9)	**0.03**
Median survival (days) CS treated vs. untreated	81 vs. 38*	>180 (N.S.)	95 vs. 55 (N.S.)	>180 (N.S.)	***P<0.05**
Overall 6-month survival	32% (11/34)	76% (32/42)	34% (9/26)	75% (9/12)	**<0.0001**

Conclusions

- We confirmed that DB is an early marker of ACLF and independently predicts a poor outcome.
- About one third of patients clinically suspected with severe ASH were misdiagnosed.
- Especially patients with Maddrey ≥32 and histologically confirmed severe ASH and DB benefited from CS treatment.
- This might explain the difference in response observed in trials assessing the value of CS for ASH.